Complete Summary

GUIDELINE TITLE

Use of calcimimetic drugs.

BIBLIOGRAPHIC SOURCE(S)

Elder G. Use of calcimimetic drugs. Nephrology 2006 Apr;11(S1):S240-4.

Elder G. Use of calcimimetic drugs. Westmead NSW (Australia): CARI - Caring for Australasians with Renal Impairment; 2006 Jan. 11 p. [15 references]

GUIDELINE STATUS

This is the current release of the guideline.

COMPLETE SUMMARY CONTENT

SCOPE

DISEASE/CONDITION(S)

- Chronic kidney diseases
- End-stage kidney disease
- Secondary hyperparathyroidism

GUIDELINE CATEGORY

Management
Treatment

CLINICAL SPECIALTY

Endocrinology
Family Practice

Internal Medicine
Nephrology
Pediatrics

INTENDED USERS

Physicians

GUIDELINE OBJECTIVE(S)

To assess the therapeutic role of cinacalcet in the following areas:

- The ability of cinacalcet to significantly reduce levels of parathyroid hormone levels calcium, phosphate and the calcium x phosphate product and the achievement of biochemical targets suggested by the Caring for Australasians with Renal Impairment and Kidney Dialysis Outcomes Quality Initiative bone guidelines
- The effectiveness of cinacalcet with increasing severity of secondary hyperparathyroidism (SHPT)
- Whether cinacalcet use alters the use of standard therapy
- Whether differences in patient-level outcome have been reported for cinacalcet versus standard therapy of SHPT
- The effects of cinacalcet treatment on bone histomorphometry, bone mineral density, fracture or surrogate endpoints of renal bone disease
- The effects of cinacalcet treatment on rates of parathyroidectomy, hospitalisation, cardiovascular or all-cause mortality or surrogate endpoints of cardiovascular disease
- The effects of cinacalcet treatment on quality of life
- The role of cinacalcet versus standard medical or surgical treatment of SHPT, based on studies published at the time of writing
- The risk of adverse side effects with cinacalcet

TARGET POPULATION

Adults and children with chronic kidney disease

INTERVENTIONS AND PRACTICES CONSIDERED

Cinacalcet

MAJOR OUTCOMES CONSIDERED

- Parathyroid hormone level
- Calcium level
- Phosphate level
- Calcium x phosphate product
- Adverse effects of treatment
- Hospitalization rate
- Mortality

METHODOLOGY

METHODS USED TO COLLECT/SELECT EVIDENCE

Searches of Electronic Databases

DESCRIPTION OF METHODS USED TO COLLECT/SELECT THE EVIDENCE

Databases searched: Medline, Embase, the Cochrane Controlled Trials Register and conference proceedings were searched for clinical trials of calcimimetics in patients with chronic kidney disease, using the terms calcimimetics, cinacalcet HC1, AMG 073 and R-568. The Cochrane Collaboration search strategy was used to identify randomised controlled trials (RCTs) of calcimimetics against placebo or other agents. Searches were conducted for clinical trials of calcimimetics and secondary hyperparathyroidism, renal osteodystrophy, bone histomorphometry, fracture, bone mineral density, calcium, phosphate, the calcium x phosphate product, parathyroid hormone, parathyroidectomy, cardiovascular disease, hospital admission, mortality, quality of life and adverse side effects. In addition, Amgen Australia forwarded a list of all peer- reviewed publications and abstracts available in their database.

Latest search date: May 2005.

NUMBER OF SOURCE DOCUMENTS

Not stated

METHODS USED TO ASSESS THE QUALITY AND STRENGTH OF THE EVIDENCE

Weighting According to a Rating Scheme (Scheme Given)

RATING SCHEME FOR THE STRENGTH OF THE EVIDENCE

Levels of Evidence

Level I: Evidence obtained from a systematic review of all relevant randomized controlled trials (RCTs)

Level II: Evidence obtained from at least one properly designed RCT

Level III: Evidence obtained from well-designed pseudo-randomized controlled trials (alternate allocation or some other method); comparative studies with concurrent controls and allocation not randomized, cohort studies, case-control studies, interrupted time series with a control group; comparative studies with historical control, two or more single arm studies, interrupted time series without a parallel control group

Level IV: Evidence obtained from case series, either post-test or pretest/post-test

METHODS USED TO ANALYZE THE EVIDENCE

Systematic Review with Evidence Tables

DESCRIPTION OF THE METHODS USED TO ANALYZE THE EVIDENCE

Not stated

METHODS USED TO FORMULATE THE RECOMMENDATIONS

Expert Consensus

DESCRIPTION OF METHODS USED TO FORMULATE THE RECOMMENDATIONS

Not stated

RATING SCHEME FOR THE STRENGTH OF THE RECOMMENDATIONS

Not applicable

COST ANALYSIS

A formal cost analysis was not performed and published cost analyses were not reviewed.

METHOD OF GUIDELINE VALIDATION

Comparison with Guidelines from Other Groups
Peer Review

DESCRIPTION OF METHOD OF GUIDELINE VALIDATION

Recommendations of Others. Recommendations regarding use of calcimimetic drugs from the following groups were discussed: Kidney Disease Outcomes Quality Initiative, British Renal Association, Canadian Society of Nephrology, European Best Practice Guidelines, and International Guidelines.

RECOMMENDATIONS

MAJOR RECOMMENDATIONS

Definitions for the levels of evidence (I–IV) can be found at the end of the "Major Recommendations" field.

Guidelines

a. Treatment with cinacalcet reduces levels of parathyroid hormone (PTH), calcium, phosphate and the calcium x phosphate product in patients with

secondary hyperparathyroidism (SHPT) due to dialysis-dependent chronic kidney disease (CKD). (Level ll evidence)

b. Treatment with cinacalcet is not reported to influence requirements for standard drug therapy of SHPT. However, a greater proportion of patients treated with the addition of cinacalcet achieve Kidney Dialysis Outcomes Quality Initiative (K/DOQI) and Caring for Australasians with Renal Impairment (CARI) target levels of PTH, calcium, phosphate and the calcium x phosphate product. (Level ll evidence)
c. When using cinacalcet, patients on dialysis with mild or moderate SHPT are more likely to achieve target levels of PTH, calcium, phosphate and the calcium x phosphate product than patients with severe SHPT. (Level ll evidence)
d. Rates of treatment withdrawal and the incidence of nausea and vomiting are higher for cinacalcet than for placebo. (Level ll evidence)

Suggestions for Clinical Care

(Suggestions are based on Level III and IV evidence)

- The use of cinacalcet in patients on dialysis is associated with a reduction in bone turnover and bone marrow fibrosis. (Level lll evidence)
- Cinacalcet should not be used in patients on dialysis with intact-PTH (iPTH) levels below the target range (Opinion). The use of cinacalcet may be associated with development of adynamic bone disease when iPTH values are < 10.6 pmol/L (< 100 pg/mL). (Level lll evidence)
- Cinacalcet therapy of SHPT may reduce rates of parathyroidectomy and fracture but has not been shown to influence hospitalisation, cardiovascular mortality, all-cause mortality or quality of life. (Post-hoc analysis of Level ll evidence)
- A therapeutic trial of cinacalcet is warranted for dialysis-dependent patients with SHPT when sustained levels of iPTH and the calcium x phosphate product remain above target levels despite optimal standard therapy. (Opinion)
- Parathyroidectomy should be considered for patients given a therapeutic trial of cinacalcet who do not achieve target levels of PTH, calcium, phosphate or the calcium x phosphate product. In particular, parathyroidectomy should be considered for patients with sustained levels of iPTH > 85 pmol/L (> 800 pg/mL), or sustained levels of iPTH > 50 pmol/L (> 470 pg/mL) in addition to levels of corrected serum calcium, phosphate or the calcium x phosphate product above the target ranges. (Opinion)
- Cinacalcet should be available for use in patients who require but are medically unfit for parathyroidectomy, or who are waiting for elective parathyroidectomy. (Opinion)

Definitions:

Levels of Evidence

Level I: Evidence obtained from a systematic review of all relevant randomized controlled trials (RCTs)

Level II: Evidence obtained from at least one properly designed RCT

Level III: Evidence obtained from well-designed pseudo-randomized controlled trials (alternate allocation or some other method); comparative studies with concurrent controls and allocation not randomized, cohort studies, case-control studies, interrupted time series with a control group; comparative studies with historical control, two or more single arm studies, interrupted time series without a parallel control group

Level IV: Evidence obtained from case series, either post-test or pretest/post-test

CLINICAL ALGORITHM(S)

None provided

EVIDENCE SUPPORTING THE RECOMMENDATIONS

TYPE OF EVIDENCE SUPPORTING THE RECOMMENDATIONS

The type of supporting evidence is identified and graded for each recommendation (see "Major Recommendations").

BENEFITS/HARMS OF IMPLEMENTING THE GUIDELINE RECOMMENDATIONS

POTENTIAL BENEFITS

Appropriate use of calcimimetic drugs in patients with chronic kidney disease and end-stage kidney disease

POTENTIAL HARMS

Adverse effects associated with use of cinacalcet

IMPLEMENTATION OF THE GUIDELINE

DESCRIPTION OF IMPLEMENTATION STRATEGY

Implementation and Audit

In Australia and New Zealand, the use of cinacalcet will depend on availability and the cost to dialysis patients. Cinacalcet should be used in conjunction with standard therapies to improve the proportion of dialysis patients who achieve target serum levels of PTH, calcium, phosphate and the calcium x phosphate product, as described elsewhere in the guidelines. Cinacalcet should be available for use by patients who require, but are medically unfit for parathyroidectomy or are waiting for elective parathyroidectomy (see Suggestions for Clinical Care).

INSTITUTE OF MEDICINE (IOM) NATIONAL HEALTHCARE QUALITY REPORT CATEGORIES

IOM CARE NEED

Living with Illness

IOM DOMAIN

Effectiveness

IDENTIFYING INFORMATION AND AVAILABILITY

BIBLIOGRAPHIC SOURCE(S)

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ADAPTATION

Not applicable: The guideline was not adapted from another source.

DATE RELEASED

2006 Apr

GUIDELINE DEVELOPER(S)

Caring for Australasians with Renal Impairment - Disease Specific Society

SOURCE(S) OF FUNDING

Industry-sponsored funding administered through Kidney Health Australia

GUIDELINE COMMITTEE

Not stated

COMPOSITION OF GROUP THAT AUTHORED THE GUIDELINE

Author: Grahame Elder

FINANCIAL DISCLOSURES/CONFLICTS OF INTEREST

All guideline writers are required to fill out a declaration of conflict of interest.

GUIDELINE STATUS

This is the current release of the guideline.

GUIDELINE AVAILABILITY

Electronic copies: Available in Portable Document Format (PDF) from the Caring for Australasians with Renal Impairment Web site.

Print copies: Available from Caring for Australasians with Renal Impairment, Locked Bag 4001, Centre for Kidney Research, Westmead NSW, Australia 2145

AVAILABILITY OF COMPANION DOCUMENTS

The following is available:

- The CARI guidelines. A guide for writers. Caring for Australasians with Renal Impairment. 2006 May. 6 p.

Electronic copies: Available from the Caring for Australasians with Renal Impairment (CARI) Web site.

PATIENT RESOURCES

None available

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